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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/763,424	01/26/2004	Stephen J. Karlik	034008-061	6792

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EXAMINER	
HADDAD, MAHER M	
ART UNIT	PAPER NUMBER
1644	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/21/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

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Office Action Summary	Application No.	Applicant(s)	
	10/763,424	KARLIK ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 October 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4, 6-8, 10-13, 15-16, 18-49 and 52-59* is/are pending in the application.

4a) Of the above claim(s) *25-45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6-8,10-13,15,16,18-24,46-49 and 52-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 10/11/06, is acknowledged.

2. Claims 1-4, 6-8, 10-13, 15-16, 18-49 and 52-59 are pending.

3. Claims 25-45 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.

4. Claims 1-4, 6-8, 10-13, 15-16, 18-24, 46-49 and 52-59 are under examination as they read on a method of promoting remyelination of nerve cells or reversing paralysis in a mammal comprising administering a remyelinating agent.

5. In view of the amendment filed on 10/11/06, only the following rejections are remained.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-3, 6-8, 10-13, 15-16, 18-24, 46-49 and 52-59 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of promoting remyelination of nerve cells or reversing paralysis in a multiple sclerosis subject comprising administering to the mammal in need thereof anti-VLA-4 antibody does not reasonably provide **enablement** for "remelination of nerve cells in a mammal", wherein the human suffers from the conditions recited in claim 3, or "reversing paralysis in a subject with a demyelination disease" in claim 46, wherein the subject with paralysis suffers for conditions recited in claim 47. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with this claim for the same reasons set forth in the previous Office Action mailed 4/11/06.

Applicant's arguments, filed 10/11/06, have been fully considered, but have not been found convincing.

Applicant points to the specification on pages 35-45 of the present specification, all of the diseases recited in the present claims, including MS, involve demyelination. Applicant concludes that a person of ordinary skill in the at would have reasonably predicted, based on the EAE animal studies, that anti-VLA-4 antiodies would promote remyelination of the nerves not only in MS but also in the other recited disease conditions.

However, the specification does not teach how to extrapolate data obtained from in EAE studies to the development of effective in vivo mammalian including human therapeutic treatment,

commensurate in scope with the claimed invention. Therefore, it is not clear that the skilled artisan could predict the efficacy of the anti-VLA-4 antibodies exemplified in the specification. While novel drugs for preventing demyelination are needed for treating clinical disorders involving the demyelinating diseases of peripheral nerve. Currently, there is no effective therapy available for hereditary motor and sensory demyelinating neuropathies (e.g., HMSN Type I) and no effective treatment for Guillain-Barre syndrome (as an example).

8. The following new ground of rejections are necessitated by the amendment submitted 11/8/06.

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1-4, 6-8, 10-13, 15-16, 18, 46-49 and 52-58 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 00/15247.

The '247 publication teaches a method of treating multiple myeloma (MM) comprising administering to an individual (human) an antibody that antagonizes the interaction of VLA-4 (alpha-4 beta1) integrin with its ligand (see published claims 1-3 in particular). The '247 publication further teaches the antibody is selected from the group consisting of a human antibody, a chimeric antibody, a humanized antibody and fragments thereof (see published claim 5 in particular). The '247 publication also teaches that the several mouse anti-VLA-4 monoclonal antibodies are capable of recognizing the a chain of VLA-4 will be useful in the methods of treatment (see page 19, lines 5-10 in particular). Furthermore, the '247 publication teaches humanized anti-VLA4 antibodies comprise three complementarity determining regions (CDR1-3) having amino acid sequences from the corresponding CDRs of a mouse 21.6 immunoglobulin light/heavy chain and a variable region framework from a human kappa light chain variable region framework sequence except in at least position the amino acid position is occupied by the same amino acid present in the equivalent position of the mouse 21.6 immunoglobulin light/heavy chain variable region framework (i.e., natalizumab) (see page 23, lines 11-26 in particular). The '247 publication teaches that the anti-VLA-4 antibody are preferably administered parentally including intravenous and subcutaneous (see page 23, lines

30-34 in particular). In addition the `247 publication teaches that the antibody includes Fab fragments, $F(ab')_2$ fragment. Also, the `247 publication teaches the compositions also comprise and additional agent such as antiinflammatories, immunosuppressants, interferons and sulfasalazine(see page 26, lines 9-20 in particular).

Claims 15 and 16 are included because the express dosage amount are material claim limitations however, the statement of the intended result of administering those amounts does not change those amounts or otherwise limit the claim.

While the `247 publication is silence with regard to "remyelination of nerve cells" and "reversing paralysis" per se; the method, the product used in the reference method are the same as the claimed method. Therefore these limitations are considered inherent properties.

The reference teachings does not explicitly teach the chronic administration of anti-VLA-4 is weekly or monthely over a period of at least six moths in claims 1 and 46 or at least one year in claims 18 and 56.

The `247 publication further teaches that that the amount of active ingredient that may be combined with the carrier materials to produce a single dosage form will vary depending upon the host treated, and the particular mode of administration. Further it should be under stood that the specific dosage and treatment regiment for any particular patient will depend upon a variety of factors and the judgment of the treating physician and the severity of the particular disease being treated. Also, the `247 publication teaches that the dosage and dose rate of the compounds effective to prevent, suppress or inhibit cell adhesion will depend on a variety of factors, such as the nature of the inhibitor, the size of the patient, the goal of the treatment, the nature of the pathology to be treated, the specific pharmaceutical composition used and the judgment of the treating physician (see page 26 lines 20-35 in particular).

It is clear that both the prior art and claimed method administer the same treatment to achieve the same results. It would be conventional and within the skill of the art to administer the anti-VLA-4 weekly or monthly for at least six months/one year. The determination of the optimal intervals of treatment is well within the purview of one of ordinary skill in the art at the time the invention was made and lends no patentable import to the claimed invention. The duration of treatment, the specific rout of administration and like factors within the knowledge and expertise of the medical practitioner. Further, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 220 F2d 454,456,105 USPQ 233; 235 (CCPA 1955). see MPEP § 2144.05 part II A.

11. Claims 1-4, 6-8, 10-13, 15-16, 18, 46-49 and 52-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Pat. No. 5,840,299.

The `299 patent teaches a method of treating central nervous system in patient (human) comprising administering to the patient a composition comprising humanized MAB 21.6 (i.e.,

anti-alpha4beta1 antibody, natalizumab) to block α4-dependent interactions of the VLA-4 receptor (see col., 14, under Methods of Treatment and claims 27-29 in particular). Furthermore, the `299 patent teaches a binding fragment of the humanized antibody. The fragments exhibit specific binding to the VLA-4 antigen, wherein humanized antibody fragments include separate heavy chains, light chains Fab, Fab', $F(ab')_2$, Fabc, and Fv (see col., 12, under Fragments of Humanized antibodies in particular). In addition, the `299 patent teaches that chimeric light and heavy chains were constructed for the mouse 21.6 $V_L$ and $V_H$ regions (see Example 2, col., 18in particular). The `299 patent also teaches the monoclonal antibody 21.6 (see col., 3, lines 36-39 in particular). The `299 patent teaches that the pharmaceutical compositions can be administered by intravenous or subcutaneous administration. (see col., 15, lines 59-65 in particular). Furthermore, the antibody is administered by intravenous infusion or subcutaneous injection at a dose from 1 to 5 mg antibody per kilo of bodyweight. The dose is repeated at interval from 2 to 8 weeks. Within this range, the preferred treatment regimen is 3 mg antibody per kilo of bodyweight repeated at a 4 week interval (see col., 16, lines 17-22 in particular).

Claims 15 and 16 are included because the express dosage amount are material claim limitations however, the statement of the intended result of administering those amounts does not change those amounts or otherwise limit the claim.

While the `299 patent is silence with regard to "remyelination of nerve cells" and "reversing paralysis" per se; the method, the product used in the reference method are the same as the claimed method. Therefore these limitations are considered inherent properties.

While the `299 publication is silence with regard to "remyelination of nerve cells" and "reversing paralysis" per se; the method, the product used in the reference method are the same as the claimed method. Therefore these limitations are considered inherent properties.

The reference teachings does not explicitly teach the chronic administration of anti-VLA-4 is weekly or monthly over a period of at least six moths in claims 1 and 46 or at least one year in claims 18 and 56.

It is clear that both the prior art and claimed method administer the same treatment to achieve the same results. It would be conventional and within the skill of the art to administer the anti-VLA-4 weekly or monthly for at least six months/one year. The determination of the optimal intervals of treatment is well within the purview of one of ordinary skill in the art at the time the invention was made and lends no patentable import to the claimed invention. The duration of treatment, the specific rout of administration and like factors within the knowledge and expertise of the medical practitioner. Further, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 220 F2d 454,456,105 USPQ 233; 235 (CCPA 1955). see MPEP § 2144.05 part II A.

Applicant's arguments, filed 10/11/06, have been fully considered, but have not been found convincing.

Applicant points that the claims now recite agents are administered chronically.

However, the determination of the optimal intervals of treatment is well within the purview of one of ordinary skill in the art at the time the invention was made and lends no patentable import to the claimed invention. The duration of treatment, the specific rout of administration and like factors within the knowledge and expertise of the medical practitioner. Further, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 220 F2d 454,456,105 USPQ 233; 235 (CCPA 1955). see MPEP § 2144.05 part II A.

12. Claims 1-4, 19-21, 49, 57 and 58 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 00/15247 in view of U.S. Pat. No 6,284,473 for the same reasons set forth in the previous Office Action mailed 4/11/06.

13. Claims 1-4, 19-20, 22-23, 49, 57 and 59 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 00/15247 or U.S. Pat. No. 5,840,299, each in view of U.S. Pat. No 6,753,135 for the same reasons set forth in the previous Office Action mailed 4/11/06.

14. Claims 1-4, 19-21, 57 and 58 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Pat. No. 5,840,299 in view of U.S. Pat. No. 6,602,885 for the same reasons set forth in the previous Office Action mailed 4/11/06.

Applicant's arguments, filed 10/11/06, have been fully considered, but have not been found convincing.

Applicant argues that the additional references cited do not remedy the deficiencies of the WO '473 and the 299 patent. Argues that there is no motivation to combine the secondary references cited by the Office.

However, based on the totality of the record as detailed above, the evidence of obviousness found in the combined reference teachings with Applicant's argument for nonobviousness. The Examiner concludes that the claimed invention encompassed by instant claims would have been obvious as a matter of law under 35 U.S.C 103(a).

14. No claim is allowed.

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

December 10, 2006

Maher Haddad

Maher Haddad, Ph.D.
Primary Examiner
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